| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 1 | BRS | L1 | 55 | clostridial adj neurotoxin | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:32 | | | 0 |
| 2 | BRS | L2 | 366 | botulinum adj (toxin or neurotoxin) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:32 | | | 0 |
| 3 | BRS | L3 | 9706 | lectin | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:33 | | | 0 |
| 4 | BRS | L4 | 61 | (galactose adj binding) same 3 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:34 | | | 0 |
| 5 | BRS | L5 | 7 | (1 or 2) same (3 or 4) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:37 | | | 0 |
| 6 | BRS | L6 | 546 | lectin same (galactose or galactosyl or aceylgalactosamine) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:37 | | | 0 |
| 7 | BRS | L7 | 2 | (1 or 2) same (6) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:38 | | | 0 |
| 8 | BRS | L8 | 2804 | erythrina or (glycine adj max) or (arachis adj hypogaea) or (bandeirea adj simplicifolia) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:38 | | | 0 |
| 9 | BRS | L9 | 111 | (erythrina or (glycine adj max) or (arachis adj hypogaea) or (bandeirea adj simplicifolia) ) same lectin | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:39 | | | 0 |

| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 10 | BRS | L10 | 0 | ((erythrina or (glycine adj max) or (arachis adj hypogaea) or (bandeirea adj simplicifolia) ) same lectin) same (clostridial adj neurotoxin) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:39 | | | 0 |
| 11 | BRS | L11 | 0 | (lectin same (recombinant or modified)) same (botulinum adj (toxin or neurotoxin)) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:39 | | | 0 |
| 12 | BRS | L12 | 56 | lectin same (arachis adj hypogaea) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:39 | | | 0 |
| 13 | BRS | L13 | 0 | (lectin same (arachis adj hypogaea)) same (clostridial adj neurotoxin) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/03/15 15:40 | | | 0 |

=> d his

(FILE 'HOME' ENTERED AT 15:42:12 ON 15 MAR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
15:42:43 ON 15 MAR 2002
L1 832 S (CLOSTRIDIAL NEUROTOXIN)
L2 18172 S (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
L3 141534 S LECTIN
L4 15375 S L3 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)
L5 2 S (L1 OR L2) AND L4
L6 2 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)
L7 9561 S L3 (P) (RECOMBINANT OR MODIF?)
L8 4 S (L1 OR L2) AND L7
L9 2 DUPLICATE REMOVE L8 (2 DUPLICATES REMOVED)
L10 1 S L9 NOT L6

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HBM

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:42:12 ON 15 MAR 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.15 | 0.15 |

FILE 'MEDLINE' ENTERED AT 15:42:43 ON 15 MAR 2002

FILE 'CAPLUS' ENTERED AT 15:42:43 ON 15 MAR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'BIOSIS' ENTERED AT 15:42:43 ON 15 MAR 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 15:42:43 ON 15 MAR 2002
COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

FILE 'SCISEARCH' ENTERED AT 15:42:43 ON 15 MAR 2002
COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R)

FILE 'AGRICOLA' ENTERED AT 15:42:43 ON 15 MAR 2002

=> s (clostridial neurotoxin)
L1 832 (CLOSTRIDIAL NEUROTOXIN)

=> s (botulinum toxin) or (botulinum neurotoxin)
L2 18172 (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)

=> s lectin
L3 141534 LECTIN

=> s l3 (p) (galactose or galactosyl or acetylgalactosamine)
L4 15375 L3 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)

=> s (l1 or l2) and l4
L5 2 (L1 OR L2) AND L4

=> duplicate remove l5
PROCESSING COMPLETED FOR L5
L6 2 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)

=> d l6 1-2 ibib abs

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:706999 CAPLUS
DOCUMENT NUMBER: 133:261538
TITLE: Use of a lectin or lectin conjugate for modulation of C-fiber activity, and therapeutic use thereof
INVENTOR(S): Foster, Keith Alan; Chaddock, John Andrew; Quinn, Conrad Padraig

HBM

PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000057897 | A1 | 20001005 | WO 2000-GB1247 | 20000331 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1165114 | A1 | 20020102 | EP 2000-914295 | 20000331 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.: GB 1999-7429 A 19990331
WO 2000-GB1247 W 20000331

AB The invention relates to the treatment of pain and to compds. that modulate C-fiber activity. In particular, the invention relates to the use of a lectin in the manuf. of a medicament for modulation of C-fiber neuron activity, and to lectin conjugates. The lectin conjugates comprise a lectin coupled to a peptide or protein, wherein the peptide or protein is substantially free of **Clostridial neurotoxin** enzyme activity. The invention also concerns methods for manufg. the conjugates.

The compds. and compns. described have particular application in the treatment of diseases of which C-fiber activity is a component. Such diseases include pain, inflammation, psoriasis and other C-fiber related conditions.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:249106 CAPLUS
DOCUMENT NUMBER: 130:276767
TITLE: Conjugates of **galactose**-binding **lectins** and **clostridial neurotoxins** as analgesics
INVENTOR(S): Duggan, Michael John; Chaddock, John Andrew
PATENT ASSIGNEE(S): The Speywood Laboratory Limited, UK; Microbiological Research Authority
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9917806 | A1 | 19990415 | WO 1998-GB3001 | 19981007 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9893574 | A1 | 19990427 | AU 1998-93574 | 19981007 |
| AU 741456 | B2 | 20011129 | | |
| ZA 9809138 | A | 19990527 | ZA 1998-9138 | 19981007 |
| EP 996468 | A1 | 20000503 | EP 1998-946571 | 19981007 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001518522 | T2 | 20011016 | JP 2000-514674 | 19981007 |

PRIORITY APPLN. INFO.: GB 1997-21189 A 19971008
WO 1998-GB3001 W 19981007

AB A class of novel agents that are able to modify nociceptive afferent function is provided. The agents may inhibit the release of neurotransmitters from discrete populations of neurons and thereby reduce or preferably prevent the transmission of afferent pain signals from peripheral to central pain fibers. They comprise a **galactose** -binding **lectin** linked to a deriv. of a **clostridial** **neurotoxin**. The deriv. of the **clostridial** **neurotoxin** comprises the L-chain, or a fragment thereof, which includes the active proteolytic enzyme domain of the light (L) chain, linked to a mol. or domain with membrane-translocating activity. The agents may be used in or as pharmaceuticals for the treatment of pain, particularly chronic pain.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

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(FILE 'HOME' ENTERED AT 15:42:12 ON 15 MAR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 15:42:43 ON 15 MAR 2002

L1 832 S (CLOSTRIDIAL NEUROTOXIN)
L2 18172 S (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
L3 141534 S LECTIN
L4 15375 S L3 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)
L5 2 S (L1 OR L2) AND L4
L6 2 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)

=> s l3 (p) (recombinant or modif?)
L7 9561 L3 (P) (RECOMBINANT OR MODIF?)

=> s (l1 or l2) and l7
L8 4 (L1 OR L2) AND L7

=> duplicate remove l8

HBM

DUPLICATE PREFERENCE IS 'CAPLUS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L8
L9 2 DUPLICATE REMOVE L8 (2 DUPLICATES REMOVED)

=> s l9 not l6
L10 1 L9 NOT L6

=> d l10 1 ibib abs

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:75297 CAPLUS
DOCUMENT NUMBER: 136:113889
TITLE: Modification of biological properties of protein toxins by stepwise iodination
AUTHOR(S): Heneine, Luiz G. D.; Heneine, Ibrahim F.
CORPORATE SOURCE: Research & Development Laboratory, Ezequiel Dias Foundation (FUNED), Belo Horizonte, 30510-050, Brazil
SOURCE: Journal of Toxicology, Toxin Reviews (2001), 20(3 & 4), 209-228
CODEN: JTTRD9; ISSN: 0731-3837
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. By gradual incorporation of stable iodine into toxins and whole venoms it is possible to abolish completely the physiol., lesional, and lethal properties of the native components. The properties of iodinated antigens and from antibodies generated by these detoxified derivs. are presented. The hapten is incorporated into tyrosyl and histidyl residues. The derivs. can be obtained in <1 h. Within the same batch of protein, there is a determinable stoichiometric ratio hapten/protein to achieve the desired **modified** properties of the deriv. The iodinating solns. are easy to prep., can be accurately standardized, and have unlimited shelf lives. The cost of the whole procedure is very low. No side-effects, local or systemic, were obsd., even with prolonged use of the derivs. The method was applied to toxic components and whole venom of the scorpion Tityus serrulatus, and the hypertensive, bradipneic, oliguric, lesional, lethal, and cytotoxic effects were completely abolished. Polyclonal antibodies generated by these iodinated antigens neutralized the virulent effects of native components and reversed the .alpha. effects of the whole venom in frog sciatic nerves. They conferred active immunization in mice, rats, guinea pigs, goats, horses, and pigeons. Crotoxin and the whole venom of Crotalus durrissus terrificus lost the lesional and lethal activity but conserved the immunogenic capacity. They produced antibodies against the native components, giving also vaccinal protection. While the virulent crotalic antigens had a cytotoxic activity, the iodinated antigens were highly mitogenic with human white cells. Repetitive sublethal doses of scorpionic, crotalic, and bothropic venoms led invariably to an amyloid-like deposit in tissues whereas the iodinated samples were ineffective. Allergenic exts. of Schistosoma mansoni can be transformed into anallergic derivs. that retain antigenic properties. Violently allergenic exts. of Ascaris lumbricoides

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suum can be completely deactivated with iodination but conserved immunol. competence. Cholera, tetanus, and **botulinum toxins**, as iodinated toxoids, had their lesional and lethal capacity completely avoided. Physiol. proteins with strong biol. activity can also be rendered innocuous. Iodinated insulin lost its capacity to lower blood glucose levels but induced high avidity antibodies in guinea pigs and rabbits. By iodination, kallikrein can be turned unable to contract rat uterus and to liberate kinins from kinninogen. **Modified** tonin do not increase the blood pressure in rats. Aq. exts. of Leptospira canis and L. icterohaemorrhagiae after iodination were innocuous to hatched eggs, and immunogenic in mice and rabbits. A **lectin** from Macrotylema axillare lost the hemaglutination capacity with only 75% of iodine satn. The deriv. was highly immunogenic in rabbits. Heavy iodination can transform self-antigens in non-self, generating antibodies in same species animals. All derivs. obtained were stable, did not show any reversion to toxicity, generated antibodies against the native antigens, and gave active protection when injected in animals. The injections were also apparently painless. The time gap between the accident and the administration of antibodies is discussed for systemic and local effects. A new schedule for immunization, only feasible with toxoided venoms, is presented. It is based on a clonal expansion induced by a small dose, followed by an exponential satn. dose of the same toxoid.

The attainment of higher levels of protecting antibodies against the native antigen in the generated sera is unmatched by other procedures. Data for practical use of iodination is presented.

REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 15:42:12 ON 15 MAR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 15:42:43 ON 15 MAR 2002

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L1          832 S (CLOSTRIDIAL NEUROTOXIN)
L2        18172 S (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
L3       141534 S LECTIN
L4        15375 S L3 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)
L5            2 S (L1 OR L2) AND L4
L6            2 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)
L7         9561 S L3 (P) (RECOMBINANT OR MODIF?)
L8            4 S (L1 OR L2) AND L7
L9            2 DUPLICATE REMOVE L8 (2 DUPLICATES REMOVED)
L10           1 S L9 NOT L6
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=> log y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 35.35 | 35.50 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -1.86 | -1.86 |